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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,370	10/03/2001	Randall K. Holmes	33,383-00	8568

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,370	HOLMES ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,24-26 and 28-43* is/are pending in the application.

4a) Of the above claim(s) *1-17,28-37 and 39-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,24-43* is/are rejected.

7)☒ Claim(s) *12,38* is/are objected to.

8)☒ Claim(s) *1-17,24-26 and 28-43* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Application/Control Number: 09/806,370
Art Unit: 1645

DETAILED ACTION

Claims 1-17, 24-26, 28-42 and 43 are pending.

Allowable Subject Matter

1. Claims 24-26 define over the prior art of record but are rejected under 35 USC 112, second paragraph. Resolution of this issue would define allowable claimed subject matter.

Election/Restrictions

1. Newly submitted claims 1-17,28-37, 39-42 and 43 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Independent claim 1 is directed to a plurality of embodiments of inventions which comprise:

a. A composition that comprises an antigen and a polynucleotide sequence that encodes the mutant cholera holotoxin (1(a-i) together with 1(b-ii))

b. A composition that comprises at least one, as well as a combination of a plurality of polynucleotides that encode a genus of antigens together with a polynucleotide sequence that encodes the mutant cholera holotoxin ; (1(a-ii) together with 1(b-ii))

c. A composition that comprises at least one, as well as a combination of a plurality of polynucleotides that encode a genus of antigens together with a mutant cholera holotoxin protein; (1(a-ii) together with 1(b-i))

All of these compositions structurally (polynucleotides structurally differ from amino acids) and functionally define independent and distinct inventions which differ from the antigen compositions that comprise one or more antigens, together with a mutant protein cholera holotoxin.

2. Additionally, a single species of a polynucleotide sequence in a plasmid that encodes HSV gD2 protein antigen together with a protein mutant cholera holotoxin, is clearly independent and distinct from compositions that comprise polynucleotides that encode antigens obtained from a fungus, bacterial or any other virus or viral antigens. What is now claimed is a genus of compositions that are directed to a genus of patentably independent and distinct inventions that structurally and functionally differ from the compositions previously examined.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, sections (a-ii and b-ii) of claims 1-17,28-37, 39-42 and 43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejections/Objections Withdrawn

3. Claim 24 objected to because of the following informalities for not reciting the term – encodes—has been obviated by amendment of the claim.

4. Claim 27 (the claimed invention was directed to non-statutory subject matter) is no longer rejected under 35 USC 101, as the claim has been canceled.

5. Claims 2,3,29,5,31,7,33,12, 38, 14,40,15,41,15,42,26, and 27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for various reasons set forth in paragraph 8, have been obviated through amendment of the claim to address the clarity of the claims.

6. All prior art rejections have been herein withdrawn in light of the amendment of the independent claim to require the combination of a mutant cholera holotoxin, the mutation being in position 29, the mutation not being the substitution of aspartic acid for glutamic acid together with at least one antigen.

Rejections Maintained

7. Claims 12 and 38 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention, is maintained for reasons of record, as subject matter incorporated by reference to a published journal article and claimed as a critical component of the invention is improper.

8. Claims 1-17, 24-42 rejected under 35 USC 112, second paragraph for reciting a position without a reference sequence is maintained in light of the fact that cholera toxin subunit A is known to have sequence variation (see Swiss Prot Accession numbers Q8vL16, Q81356, and P01555.)

Response to Arguments

9. The rejection of claims 12 and 38 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is traversed on the grounds that the sequence for HSV gD2 antigen was known at the time of filing and therefore the claimed antigen compositions are enabled.

10. It is the position of the examiner that the attempt to incorporate subject matter into this application by reference to Pachuk et al, in Example 13, pages 109-113 of the instant specification is improper because an effective Declaration has not been submitted . The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material **consists of the same material** incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ

163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

What is now claimed is an antigenic composition, the plasmid being the antigen; Applicant has not shown that any plasmid comprising any coding sequence of HSV gD2 antigen would function as a vaccine antigen. The specification fails to provide an enabling disclosure for the preparation and use of any compositions, including viral vector compositions comprising nucleic acids encoding HSV gD2 antigens because it fails to provide adequate guidance regarding how one would have prepared a nucleic acid which when introduced into a host would induce an immune response against the protein encoded by said nucleic acid. In contrast to direct protein immunogens, nucleic acids are required to target appropriate cell types within a host, become transcriptionally active, appropriately process any encoded proteins and present such proteins to the host in a manner suitable for recognition by the host's immune system. Such a **"gene therapy"** approach to epitope delivery suffers from all the limitations associated with gene therapy technology. However, as of 12/95, the artisan did not accept, in the absence of suitable and particular guidance, that such could have been accomplished without having had to have exercised undue experimentation. See e.g. NIH Report Reference. The enablement rejection is maintained for reasons of record.

11. The rejection of claims 1-17, 24-42 under 35 USC 112, second paragraph for reciting a position without a reference sequence is maintained in light of the fact that cholera toxin subunit A is known to have sequence variation (see Swiss Prot Accession numbers Q8vL16, Q81356, and P01555) is traversed on the grounds that the specification refers to Mekalanos et al, 1983, Nature.

12. It is the position of the examiner that sequence variation for cholera toxin is known in the art (see Swiss Prot Accession numbers Q8vL16, Q81356, and P01555) and if the sequence of Mekalanos et al is the reference sequence intended, resolution of improper incorporation by reference to critical subject matter could be obviated through submission of an effective Declaration. It is not clear whether the A-subunit number starts with or without the signal sequence, as the type of A-subunit could be in the pro-toxin form or in the form where the signal sequence has been cleaved; based upon these two situations, the numbering from the N-terminal of the protein antigen would result in a different position for substitution of the amino acid. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. **Applicant is required to amend the disclosure to include the material incorporated by reference.** The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material **consists of the same material** incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

New Claim Limitations/New Grounds of Objection/ Rejection

Claim Objections

13. Claims 12 and 38 are objected to because of the following informalities: Claims 12 and 38 depend from sections of the independent claim which have been withdrawn from

consideration. Amendment of claims 12 and 38 into independent form could obviate this objection. Appropriate correction is required.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure

15. Jobling et al (J. of Bacteriology, 2001) is cited to show characterization of site-directed mutants of cholera toxin.

16. Lobet et al (1991) is cited to show site-directed mutagenesis of E.coli heat labile enterotoxin, and suggests the mutagenesis of glutamic acids in the A1 subunit, at conserved positions 15, 29, 110, 112 and 159; as well as teaches a correlation between glutamic acid positions in both E.coli heat labile enterotoxin and cholera toxin (see abstract page 2870; page 2875, col. 1, second paragraph, last sentence bridging over to col. 2, first sentence).

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
March 5, 2003

L. F. Smith

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